MEDICAL PHARMACIES TABLET

Drug information and news for health care providers

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INSULIN USE FOR TYPE 2 DIABETES MANAGEMENT

This issue of the *Tablet* and the next one will focus on the use of insulin. In this issue we will discuss utilization of insulin for treatment of type 2 diabetes. The next issue will focus on safety issues associated with the use of insulin.

WHEN SHOULD INSULIN BE USED TO TREAT TYPE 2 DIABETES?

The initiation of insulin in a person with type 2 diabetes should never be viewed as a "last resort." Type 2 diabetes is a progressive disease and, in fact, insulin has the advantage of being the only anti-diabetes agent with a flexible regimen and no dose ceiling.[1] According to the most recent Canadian Diabetes Association guidelines, insulin should be used when:[1,2]

- oral antihyperglycemics alone are not enough to achieve glycemic control or
- the patient is experiencing symptomatic hyperglycemia with metabolic decompensation and
- as an alternative in combination with oral antihyperglycemic agents (e.g., metformin) when hemoglobin A1C (A1C) is ≥ 8.5%.

HOW SHOULD THE INITIAL INSULIN REGIMEN BE SELECTED?

There are three primary insulin regimens that are normally considered for initial use.[2] (If pioglitazone or rosiglitazone are being used, they should be discontinued prior to addition of insulin.[2])

1. **Background (basal) insulin added to oral agents:** This simple addition of one or two injections daily is especially desirable if the patient is feeling overwhelmed, is fearful of injections, and/or has mostly elevated fasting plasma glucose.
2. **Premixed insulin:** This addition is especially desirable if the patient is opposed to more than two injections a day and has consistent mealtimes and food intake. It is appropriate for patients with elevated fasting and/or postprandial plasma glucose.
3. **Background (basal) and mealtime (bolus) insulin:** This addition is especially desirable if tight control of glucose levels is required with a flexible schedule. This regimen is appropriate for patients with elevated fasting and/or postprandial plasma glucose.

WHAT INSULIN REGIMEN SHOULD BE USED WHEN ADDING TO AN ORAL ANTIHYPERGLYCEMIC AGENT?

Most often, a single injection of intermediate-acting (NPH) or a long-acting insulin analogue (insulin glargine or insulin detemir) is added to oral antihyperglycemic agent(s).[1] This combination often controls glucose levels effectively with relatively small doses of insulin.[1] And this approach may cause less weight gain and pose reduced risk of hypoglycemia than stopping oral antihyperglycemic agents completely and starting insulin alone. This is especially true when insulin is added to metformin.[1] Insulin regimens should be designed to achieve good metabolic control while minimizing risk of hypoglycemia.[1]

As type 2 diabetes progresses, and glycemic control becomes more difficult, insulin requirements are likely to increase. This may indicate the need for additional doses of basal insulin and, potentially, the need for doses of regular or short-acting insulin as mealtime boluses or as part of a premixed regimen.[1] At this point, oral insulin secretagogues (e.g., sulfonylureas, meglitinides) are usually discontinued. If metformin is being used, it should be continued to contribute to glycemic control and reduce risk of weight gain and hypoglycemia. An excellent summary of "Examples of Insulin Initiation and Titration Regimens in People with Type 2 Diabetes" can be found on the Canadian Diabetes Association Guidelines website at http://guidelines.diabetes.ca/Browse/Appendices/Appendix3.

WHAT APPROACHES CAN I USE TO HELP ADVOCATE FOR THE USE OF INSULIN FOR INDIVIDUALS WHO WOULD BENEFIT?

As we are all aware, many people have a fear of needles and will see the move to insulin as a failure on their part. Following are some tips when advocating for the use of insulin:[2]

- Assure the patient that type 2 diabetes is a progressive disease and the key to preventing health issues is to keep blood sugar under control. It is normal to require insulin at some point in the journey, and it is the best medication available for controlling blood sugar.
- Start to discuss insulin early in the course of treatment to correct false misconceptions and negative perceptions.
- Discuss the "newer" insulin devices and supplies such as the pen and smaller, finer needles.
- Consider suggesting a one-month trial. MPT

Prefilled Insulin Pens

Prefilled insulin pens are now included as benefits under many provincial drug plans including the Ontario Drug Benefit program. Many long-term care homes are transitioning to prefilled insulin pens from other dosage forms of insulin for safety and convenience.

Available prefilled insulin pens include:

- Rapid-acting insulins: Humalog® KwikPen® (insulin lispro), NovoRapid® FlexTouch® (insulin aspart), Apidra® SoloSTAR® (glulisine)
- Short-acting insulins: Humulin® R KwikPen®
- Premixed insulins: Humalog® Mix25 KwikPen®, Humalog® Mix50 KwikPen®
- Long-acting insulins: Levemir® FlexTouch® (insulin detemir), Lantus® SoloSTAR® (insulin glargine).

Considerations and tips for choosing and using disposable prefilled insulin pens or reusable insulin cartridge pens:

- With the use of prefilled insulin pens, the chore of loading a reusable insulin pen with a new cartridge is eliminated.
- Needles must always be disposed of in sharps containers; however, disposable syringes (without the needles) should be disposed of in an approved waste container if it still contains drug, or in a garbage container if no drug is present.
- Studies have shown that compared with traditional delivery methods (i.e., vial and syringe), pen devices are associated with improved costs of care, less reported injection pain, improved accuracy of dose, and improved adherence to treatment. Pens are also easier to use for people with dexterity issues.
- Note that all intermediate-acting (i.e., Humulin® N, Novolin® ge NPH) and premixed insulins must be resuspended before use (i.e., roll the pen and cartridge in palm of hand ten times and invert it 180º ten times).

An excellent Insulin Pen Start Checklist resource can be found on the Canadian Diabetes Association website at http://guidelines.diabetes.ca/BloodGlucoseLowering/InsulinChecklist.

Glucagon-Like Peptide-1 Agonists (GLP-1 agonists)

GLP-1 agonists (also known as incretin mimetics) currently available in Canada are exenatide (Byetta®) and liraglutide (Victoza®). These drugs, which are injected subcutaneously, are structurally similar, but not exactly the same, as the naturally occurring GLP-1 agonist.[3] They have been modified so that the half-life of the drug is longer than that of the naturally occurring hormone. In the body, GLP-1 is produced in response to food intake and stimulates glucose-dependent insulin release while suppressing postprandial glucagon secretion. It also delays gastric emptying, which increases satiety (a feeling of fullness in the stomach). The drugs reduce A1C by 1% to 1.5% on average and also help patients to lose weight.[3]

Indications

Exenatide and liraglutide are indicated for the treatment of adults with type 2 diabetes to improve glycemic control in combination with:[4,5]

- Metformin, when diet and exercise plus maximal tolerated dose of metformin do not achieve adequate glycemic control
- Metformin and a sulfonylurea, when diet and exercise plus dual therapy with metformin and a sulfonylurea do not achieve adequate glycemic control
- For exenatide: Insulin glargine (with or without metformin) to improve glycemic control in patients with type 2 diabetes when insulin glargine (with or without metformin) in addition to diet and exercise does not provide adequate glycemic control
- For liraglutide: Metformin and a basal insulin, when diet and exercise plus dual therapy with the GLP-1 agonist and metformin do not achieve adequate glycemic control.

Dose & Administration

Exenatide should be initiated at 5 µg per dose injected subcutaneously twice daily (any time within the 60-minute period before the morning and evening meal, at least six hours or more apart) in patients with type 2 diabetes who are already receiving metformin, a sulfonylurea, or a combination of metformin and a sulfonylurea. The dose may be increased to 10 µg twice daily after one month of therapy to further improve glycemic control, as tolerated. The maximum dose is 10 µg twice daily. If no improvement in glucose control is seen after three to four months, alternative therapies should be considered.

Liraglutide should be injected subcutaneously at an initial dose of 0.6 mg once daily for at least one week. After one week, the dose should be increased to 1.2 mg once daily. Based on clinical response and after at least one more week, the dose can be increased to 1.8 mg once daily to achieve maximum efficacy for glycemic control. DN

This review is not comprehensive. Please refer to Byetta® and Victoza® product monographs for more comprehensive information, including precautions, adverse reactions, and drug interactions.

References:

1. Harper W, Clement M, Goldenberg R, et al. Pharmacologic Management of Type 2 Diabetes. CDA Clinical Practice Guidelines. Available online at http://guidelines.diabetes.ca/Browse/Chapter13. Accessed Oct. 1, 2014.
2. Canadian Agency for Drugs and Technology in Health (CADTH). Guide to Starting and Adjusting Insulin for Type 2 Diabetes. Available online at http://www.cadth.ca/en/products/optimal-use/self-monitoring/tools/guide-to-starting-insulin-print. Accessed Oct. 1, 2014.
3. PL Detail-Document, Drugs for Type 2 Diabetes. Pharmacist's Letter/Prescriber's Letter. October 2014. Available online at http://pharmacistsletter.therapeuticresearch.com/pl/ArticleDD.aspx?nidchk=1&cs=&s=PL&pt=3&fpt=2&segment=4620&dd=280805. Accessed Oct. 16, 2014.
4. Byetta® product monograph. e-CPS 2014.
5. Victoza® product monograph. e-CPS 2014.